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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/526,858 | 03/02/2005 | Hiroyoshi Hidaka | 8279.829USWO | 5428 |

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| EXAMINER | |
|---|---|
| GEMBEH, SHIRLEY V | |
| ART UNIT | PAPER NUMBER |
| 1628 | |
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| 02/28/2011 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/526,858 | HIDAKA ET AL. | |
| | Examiner | Art Unit | |
| | SHIRLEY V. GEMBEH | 1628 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *03 January 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *15,16 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,16 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Response to Arguments*

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/3/11 has been entered.

1. The response filed on **1/3/11** has been entered.

**2.** Applicant's arguments filed 1/3/11 have been fully considered but they are not deemed to be persuasive.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 15-16 and 27 are pending in this office action.

***Maintained Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 15-16 and 27 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hidaka et al. (US Patent 5,972,976) in view of Goodman and Gilman (1996) as made of record in Paper No. 20100803 and as follows.

Hidaka et al. teach a pharmaceutical composition for treating malignant tumor (see col. 1 lines 13+ such as colon cells, see col. 28, lines 40-45) with a compound of formula I wherein the compound is E) -4- [2- [2- [N-acetyl-N- [(p- methoxyphenyl )sulfonyl] amino] phenyl] ethenyl] pyridine 1 – oxide wherein the Hidaka teaches that the compound be administered at effective doses of 25, 50, 100 and 200 mg/kg (see col. 29, tables 3 and 4) with a survival rate of 100%.

Although Hidaka fails to teach combinations with other known anticancer agents such as cisplatin, Goodman and Gilman teach that the antitumor agents cisplatin and carboplatin may be combined with other anticancer drugs for the treatment of cancers, such as breast, ovary and lung (see pages 1229 and 1230) wherein Goodman and Gilman specifically teach that "drugs are generally more effective in combination and may be synergistic..." Further Goodman and Gilman teach that the usual intravenous dose of cisplatin is 20 $mg/m^2$ (see page 1270 under subsec. Therapeutic uses).

Therefore one of ordinary skill in the art would have been motivated to combine a known anticancer drug employed in the treatment of breast cancer with the newly found drug of Hidaka that is capable of treating the same type of disease via a different mechanism because Goodman and Gilman teach the combination of anticancer drugs, which such may result in a synergistic effect because of their different mechanistic route (see page 1230 of Goodman and Gilman, para. 3).. Accordingly, in *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980), the court held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose (i.e., treating cancer) in order form a third composition that is to be used for the very same purpose since the idea of combining them flows logically from their having been individually taught in the prior art. Additionally because the compound (E)-4-[2-[2-[N-acetyl-N-[(p-methoxyphenyl)sulfonyl]amino]phenyl]pyridine 1-oxide may also be administered at 25, 50, 100 and 200 mg/kg (see col. 29, tables 3 and 4) with a survival rate of 100%. Goodman and Gilman teach that the usual intravenous dose of cisplatin is 20 mg/m$^2$ (see page 1270 under subsec. Therapeutic uses) therefore it is reasonable that these effective amounts taught by both Hidaka and Goodman and Gilman would necessarily result in a synergistic effect absent factual evidence to the contrary. The examiner is unable to determine whether the prior art disclosures actually possesses the characteristic of synergism. Under such circumstances, where the product seems to be identical, then the burden shifts to applicant to provide evidence that the prior art would neither anticipate nor render obvious the claimed invention. Note the case law of In re Best 195 USPQ 430, 433 (CCPA 1977).

Applicant argues that "there is no particular guidance in Goodman and Gilman as to particular mechanisms, biochemical interactions, or other factors, which one might target, so as to lead one of skill in the art to combine the compounds as required by claim 27. Rather, the reference only generally acknowledges that a number of factors must be taken into account when developing regimens for clinical use. And given the vast number of compounds that one might attempt to combine, there is no reason that one of skill in the art would have arrived at selecting the claimed combination of compounds required by claim 27, much less have expected success in doing so" and also argues that "Claim 27 is directed to a method for treating a patient suffering from at least one malignant tumor selected from the group consisting of blood cancer, leukemia, human colon adenocarcinoma, gastrointestinal cancer, lung caner, breast cancer, and prostate cancer. The method comprises administering a therapeutically effective amount of (E)-4- [2- [2- [N-acetyl-N- [(p-methoxyphenyl)sulfonyl] amino] phenyl]ethenyl]pyridine 1 -oxide (referred to as HMN-214 hereinafter) or a pharmaceutically acceptable salt thereof in combination with cisplatin. Applicant further argues that claim 27 also recites that the therapeutically effective amount of (E)-4-[2-[2-[N-acetyl-N-[(p-methoxyphenyl)sulfonyl]amino]phenyl]pyridine 1-oxide with cisplatin gives a synergistic inhibitor/effect". Applicant further argues that the "T/C value is an indicator that shows how long survival times of animals of a treated group are extended compare to those of a control group" and that the values reported reflects synergism.

In response careful consideration have been given to Applicant's argument and found not persuasive for several reasons:

1) the claims do not recite any dosage amount only an effective amount of (E)-4-[2-[2-[N-acetyl-N-[(p-methoxyphenyl)sulfonyl]amino]phenyl]pyridine 1-oxide administered simultaneously with cisplatin. Page 23 of the specification, Table 1, as asserted by applicant shows a dosage of 25, 50 and 100 mg/Kg administered to a mice, however the prior Hidaka art teaches that the compound (E)-4-[2-[2-[N-acetyl-N-[(p-methoxyphenyl)sulfonyl]amino]phenyl]pyridine 1-oxide may also be administered at 25, 50, 100 and 200 mg/kg (see col. 29, tables 3 and 4) with a survival rate of 100%. Goodman and Gilman teach that the usual intravenous dose of cisplatin is 20 $mg/m^2$ (see page 1270 under subsec. Therapeutic uses). It is *prima facie* obviousness to select a known material based on its suitability for its intended use. *See Sinclair & Carroll Co. v. Interchemical Corp.*, 325 U.S. 327, 65 USPQ 297 (1945). Also, established precedent holds that it is generally obvious to add known ingredients to known compositions with the expectation of obtaining their known function. See, e.g., *In re Linder*, 457 F.2d 506, 507 (CCPA 1972); see also *In re Dial*, 326 F.2d 430, 432 (CCPA 1964). Therefore, one of ordinary skill in the art based on the effective amounts discussed by the prior art would be motivated to administer the amounts taught by Hidaka and Goodman and Gilman with a reasonable expectation of success because the same amounts are disclosed by the specification and therefore would achieve an additive effect when combined at the effective doses taught by the prior art. Thus one of ordinary skill in the art following the guidance of the prior art references would reasonably use the effective amounts taught by the specification to achieve synergistic result.

2) it is well known in the art that co administration of drugs give additive effect especially when the two drugs have different binding sites as taught by Goodman et al. (see page 1230 of Goodman and Gilman, para. 3). Even though the specification is not read in light of the claims, page 1 bridging page 2 specifically discusses that treating cancer via adjuvant chemotherapy by the combination of plural tumor agents acting through different mechanism would be useful to attain better therapeutic results which is the same as taught by Goodman and Gilman (as discussed above).

Examiner again suggests deleting the term "effective amount" to a specific dosage amount that actually yields synergistic effect. Also Applicant can show a trend that is commensurate in scope with the claims and show that the unexpected result is truly unexpected.

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, BRANDON FETTEROLF can be reached on 571-272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. V. G./
Examiner, Art Unit 1618
2/15/11
/Brandon J Fetterolf/

Supervisory Patent Examiner, Art Unit 1628